REMARKS

Summary of the Invention

The invention features a method for treating a patient suffering from aphthous that involves orally applying a composition consisting essentially of a steroid and a TNF-α inhibitor to the aphthous.

Summary of the Office Action

Claim 1 is pending and stands rejected under 35 U.S.C. § 112, first paragraph, for overbreadth. Claim 1 also stands rejected under 35 U.S.C. § 102 over Andrulis et al. (U.S. Patent No. 5,654,312; hereinafter "Andrulis"), and under 35 U.S.C. § 103 over the'312 patent in combination with Quinn et al. (Stomatitis, Nov. 29, 1995; hereinafter "Quinn"). By this reply, Applicant adds new claims 2-6, and addresses each of the Examiner's rejections below.

Support for the Amendments

Support for new claims 2-6 is found in the specification on page 3, line 10, through page 4, line 6. No new matter is added by the amendments.

Rejection under 35 U.S.C. § 112, first paragraph

Claim 1 is rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement.

The Examiner states that "the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims." Applicant respectfully traverses this rejection.

The first issue is whether Applicant must provide a list of steroids and TNF-α antagonists sufficient to define the class of compounds that can be used in a method of treating aphthous. The Examiner states that "Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation." The Examiner also notes that the "examples [provided] are neither exhaustive, nor define the class (e.g., structure) of compounds required." The courts held in *DeGeorge v. Bernier* (768 F.2d 1318, 226 USPQ 758 (Fed. Cir. 1985)) that "[a] patent must contain a description that enables one skilled in the art to make and use the claimed invention...' An inventor need not, however, explain every detail since he is speaking to those skilled in the art.'" A patent specification does not need to describe exactly all the subject matter that is claimed. (*In re Daniels*, 114 F.3d 1452, 46 U.S.P.Q.2d 1788 (Fed. Cir. 1998); *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 227 U.S.P.Q. 117 (Fed. Cir. 1985).) Rather, Applicant needs only communicate to those skilled in the art that the claimed subject matter is intended to be part of their invention. In applying this standard, the Federal Circuit has held that the specification must convey with reasonable clarity to a skilled artisan that the inventor "was in possession of the invention" at the

time of filing. (*Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991).) Moreover, in *Regents of the University of California v. Eli Lilly and Co.* (119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997)), the Federal Circuit acknowledged that "every species in a genus need not be described in order that a genus meets the written description requirement." (43 U.S.P.Q.2d at 1405 (citing *Utter v. Hiraga*, 845 F.2d 993, 6 U.S.P.Q.2d 1709 (Fed. Cir. 1988) ("A specification may, within the meaning of § 112, ¶ 1, contain a written description of a broadly claimed invention without describing all species that claim encompasses.")) The *Lilly* court further acknowledged that "it may not be necessary to enumerate a plurality of species if a genus is sufficiently identified ... by other appropriate language." (*Lilly*, 119 F.3d at 1569.)

Applicant has plainly met these standards. One skilled in the art would immediately recognize what was meant by a "steroid" and a "TNF-α antagonist", as described in the specification, because such compounds were well known in the art at the time the application was filed. Therefore, practicing the claimed method would not require undue experimentation, as stated by the Examiner, because these compounds are well-defined in the art and would be known to the skilled artisan by the terminology given in Applicant's specification.

The real issue is whether identifying the various combinations of orally applied steroids and TNF-α antagonists effective for treating aphthous constitutes undue experimentation. Case law on this issue clearly indicates that although some

experimentation may be required to practice the invention, this is not justification for rejecting a claim for lack of enablement (*Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 USPQ 81 (Fed. Cir. 1986)). In *Hybritech v. Monoclonal Antibodies*, the requirement that antibodies be tested for binding to an antigen was held not to support a lack of enablement rejection; experimentation admittedly was required, but it was routine, not undue. Applicant's method involves providing a composition containing a steroid and a TNF-α antagonist for oral application to treat aphthous. While Applicant's specification may not identify an "exhaustive" list of combinations, the process of combining a steroid with a TNF-α antagonist and testing the combination for its ability to treat aphthous would simply require routine experimentation. As is discussed above, this type of experimentation is not a bar to patentability. Therefore, based on the above remarks, Applicant respectfully requests that the rejection of claim 1 under 35 U.S.C. § 112, first paragraph, be withdrawn.

Rejection under 35 U.S.C. § 102(b)

Claim 1 is rejected under 35 U.S.C. § 102(b) for anticipation in view of Andrulis. The Examiner states that Andrulis "discloses a method of treating ulceration of the mouth employing thalidomide (a TNF antagonist) and prednisone (a steroid)." Applicant respectfully traverses the rejection.

The M.P.E.P. § 2131 states

> A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. Of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Contrary to the Examiner's statement, Andrulis fails to teach or suggest every element of present claim 1. Claim 1 recites the treatment of a patient suffering from aphthous by orally applying a composition consisting essentially of a steroid and an inhibitor of TNF-α (i.e., both components are administered in one composition at the same time). Andrulis provides a summary of three studies: one by Saylan and Saltik, one by Torras et al., and one by Denman et al., wherein patients suffering from oral aphthae were treated with thalidomide. In the Saylan and Saltik and Torras et al. studies, thalidomide was used alone to treat aphthae. When describing the Denman et al. study, Andrulis states that "39 patients with Behcet's syndrome...[were treated with] thalidomide...[and that] [c]oncomitant treatment in this patient group included 10 patients on prednisone, 3 on azathioprine and 1 on cyclosporin" (See column 3, line 66, through column 4, line 1). Andrulis clearly fails to teach or suggest (vis a vis Denman et al.) the treatment of aphthous lesions in patients by either orally applying a composition or by treating the patients with a single composition consisting essentially of a steroid and an inhibitor of TNF-α (i.e., a composition in which both components are present in the same composition and administered at the same time). In fact, it is apparent from the description provided by Andrulis that the patients were not treated with a single

composition consisting essentially of thalidomide and prednisone, but with many different compositions that included these two components in the hope that a beneficial outcome may be observed in the patients. Therefore, contrary to the Examiner's statement, Andrulis clearly fails to teach each and every element of claim 1 as required by the M.P.E.P. § 2131. Absent a teaching of each and every element, there can be no anticipation (*Verdegaal Bros. v. Union Oil Co. Of California*). Based on the above remarks, Applicant respectfully requests that the rejection of claim 1 under 35 U.S.C. § 102(b) be withdrawn.

Rejection under 35 U.S.C. § 103(a)

Claim 1 is rejected under 35 U.S.C. § 103(a) over Andrulis in combination with Quinn. The Examiner states that Andrulis

> teaches that TNF alpha antagonists (PTX and thalidomide) and glucocorticoids (dexamethasone) are useful in treating dermatoses with an autoimmune or inflammatory basis...[and that] Quinn...teaches that aphthae is caused by an underlying autoimmune mechanism. It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ TNF antagonist [sic] and steroids in the treatment of aphthae.

Applicant respectfully traverses this rejection.

The M.P.E.P. § 2143.02 states

> A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock,*

> *Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984).

Andrulis states that "[t]halidomide has...been used successfully to treat Behcet's syndrome...[however] [s]teroids proved to be only of limited usefulness in treating Behcet's..." (See column 3, lines 39-50.) Furthermore, Andrulis describes a study by Denman et al. (Rev. Med. Int. 14:495, 1993) in which 39 patients with Behcet's syndrome were treated with thalidomide. Andrulis notes that of these patients, concomitant treatment with prednisone occurred in 10 patients, while 3 patients were also treated with azathioprine, and 1 with cyclosporin. Yet, Andrulis states that "mucosal lesions healed in all patients." (See column 4, lines 1-2 of Andrulis.) This description would fail to indicate to one skilled in the art that the combination of thalidomide with prednisone provided any substantial benefit over the use of thalidomide with either azathioprine or cyclosporin. Furthermore, this description, in combination with the statement that steroids were not useful for treating Behcet's syndrome, would teach away from the specific use of a steroid in combination with an inhibitor of TNF-α, as is presently claimed.

The Examiner also relies on Quinn, which teaches that

> Treatment attempts over the years have been imaginative and largely unsuccessful...[and that] [m]edical treatment has ranged from antiobiotics, immunosuppressants and yogurt, to Lactobacillus capsules. An oral suspension of tetracycline...has shown good results and topical steroids..may shorten the duration significantly if started

> early. Systemic steroids are often needed to control major aphthae." (See page 4, ¶7; Emphasis added.)

Quinn, like Andrulis, teaches that treatment of aphthae has been largely unsuccessful. Even treatment with topical steroids does not guarantee success. Quinn indicates that systemic administration of steroids seem to control major aphthae. Both Andrulis and Quinn, however, clearly teach away from the topical use of steroids and TNF-α inhibitors to treat aphthae. One skilled in the art would lack any motivation to treat aphthae with a combination of a TNF-α antagonist and a steroid, as is recited in present claim 1. Even if one skilled in the art, upon reading Quinn and Andrulis, would be motivated to treat aphthae with a combination of a TNF-α antagonist and a steroid, there is no suggestion that these compounds would be administered by oral application, as is presently claimed. Quinn clearly indicates that systemic administration of steroids is the preferred method (see page 4, ¶7, of Quinn), while Andrulis suggests that topical administration is the preferred method (See column 10, line 3, of Andrulis). Accordingly, Applicant submits that the present invention would not be obvious in light of Andrulis and Quinn due to the obvious confusion and teaching away from the use of steroids in the treatment of aphthae and the lack of any guidance regarding oral application of these compounds. Therefore, the combination of Andrulis and Quinn clearly fails to teach or suggest the claimed invention. Accordingly, Applicant respectfully requests that the rejection of claim 1 under 35 U.S.C. § 103(a) be withdrawn.

CONCLUSION

Applicant submits that the claims are in condition for allowance, and such action is respectfully requested. Enclosed is a petition to extend the period for replying for three months, to and including December 19, 2002. Also, enclosed is a check for $140.00 for excess claim fees as required by 37 C.F.R. 1.16(d). If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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